Review and Update

Primary Coronary Angioplasty

in Patients with Acute Myocardial Infarction

Jeffrey J. Popma, MD
Ya Chien Chuang, PhD
Lowell F. Satler, MD
Benjamin Kleiber, BA
Martin B. Leon, MD

In some patients with acute myocardial infarction, thrombolytic therapy may be limited by its failure to reperfuse the occluded artery, by recurrent ischemia (despite initially successful reperfusion), and by major hemorrhagic complications. Primary coronary angioplasty may circumvent these limitations.

This article reviews the results of primary angioplasty reported in patients with myocardial infarction and makes recommendations for its use. The review includes pertinent articles found in the English language literature from July 1987 to July 1993 on MEDLINE.

Nonrandomized series of primary angioplasty in acute myocardial infarction have demonstrated high procedural success rates (86% to 99%) and infrequent recurrent ischemia (4%). Two randomized trials comparing primary angioplasty and thrombolytic therapy have shown that primary angioplasty results in lower mortality, less recurrent ischemia, shorter length of hospital stay, and improved left ventricular function. Two other randomized studies have shown little benefit from primary angioplasty on myocardial salvage, recurrent ischemia, or ventricular function. One major limitation of primary angioplasty is that it requires 24-hour availability of a catheterization laboratory and experienced surgical personnel.

Primary angioplasty may be the preferred approach in patients with extensive myocardial infarction who have immediate (<120 min) access to a cardiac catheterization laboratory with experienced personnel. Patients having 1) contraindications to thrombolytic therapy, 2) cardiogenic shock, 3) prior coronary bypass surgery, or 4) "stuttering" onset of pain may also benefit from primary angioplasty. Poor candidates for this procedure are those with a small myocardial infarction, those in whom undue delays in access to a cardiac catheterization facility would be expected, or those with complex coronary anatomy, including left main coronary artery disease. ***(Texas Heart Institute Journal 1994;21:148-57)***

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From: *The Department of Internal Medicine (Cardiology Division), Washington Hospital Center, Washington, DC 20010*

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Address for reprints: *Jeffrey J. Popma, MD, Washington Hospital Center, 110 Irving Street, N.W., Suite 4B-1, Washington, DC 20010*

Over the past decade, the evolution of mechanical and pharmacologic reperfusion therapy has dramatically altered the management of patients with acute myocardial infarction. To date, 2 major competing strategies of coronary recanalization have emerged as the most effective treatments for patients with evolving myocardial infarction (Fig. 1). The 1st approach uses systemic administration of a thrombolytic agent (e.g., tissue plasminogen activator [t-PA], streptokinase, or anistreplase) to achieve recanalization of infarct-related arteries. This approach has the advantages of widespread availability and documented benefits in both low- and high-risk patient subsets.[1,2] Despite its expanding use, thrombolytic therapy has important limitations, including failure to reperfuse the occluded segment in 20% to 40% of patients,[3-5] reocclusion despite successful initial reperfusion in an additional 12%,[6] and the infrequent (<1%) but often devastating occurrence of intracranial hemorrhage and other major bleeding complications.[1,2,7] Relative and absolute contraindications to thrombolytic therapy are also frequently noted (e.g., severe hypertension, recent cerebrovascular accident, recent surgery, or history of gastrointestinal hemorrhage).[8]

As an alternative to thrombolytic therapy, primary coronary angioplasty may be useful in patients with acute myocardial infarction. High patency rates (>90%) can be achieved using primary angioplasty in such patients. Moreover, the residual coronary stenoses often noted after thrombolytic administration can be treated effectively, potentially reducing the risk of late reocclusion.[9,10] In the absence of concomitant fibrinolysis, the complications generally associated with immediate angioplasty after thrombolytic administration (e.g., hemorrhagic myocardial

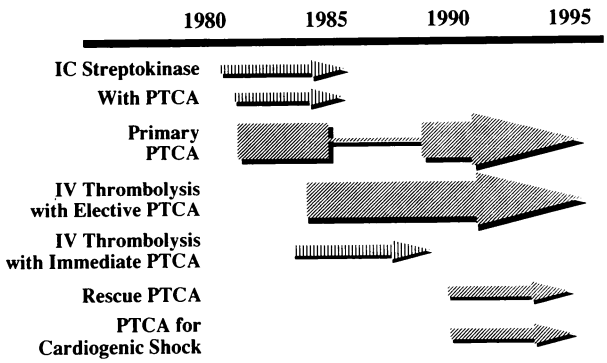

Fig. 1 *Schematic representation of the historical development of pharmacologic and mechanical reperfusion strategies used in patients with acute myocardial infarction.*

IC = intracoronary; IV = intravenous; PTCA = percutaneous transluminal coronary angioplasty

infarction, bleeding complications, and thrombin-mediated platelet aggregation)[3-5] can be avoided. Patients with contraindications to systemic thrombolysis can also be managed effectively with primary angioplasty. In spite of these benefits, the use of primary coronary angioplasty may be limited in patients with acute myocardial infarction by its lack of regional availability and also by its requirement for 24-hour accessibility to a catheterization laboratory and to operating room personnel.

A number of clinical centers in the United States and Europe have remained firmly committed to the use of primary coronary angioplasty for acute myocardial infarction; on the basis of results obtained in these nonrandomized series,[11-21] several randomized trials of primary angioplasty and thrombolytic therapy have been performed.[9,10,22] Whereas some randomized studies have shown a significant reduction in the frequency of recurrent ischemic events after primary angioplasty,[9,10] others have suggested that the differences in these approaches may be less pronounced.[22,23] This review evaluates the current indications for primary coronary angioplasty based on the results of clinical series available to date.

Historical Perspective

Soon after it was observed through angiography that an occlusive coronary thrombus was present in more than 90% of patients with acute myocardial infarction,[24] clinical investigators demonstrated the feasibility and safety of pharmacologic (intracoronary streptokinase) and mechanical (coronary angioplasty) methods of infarct-related artery recanalization; these techniques were used alone[25,26] and in combination.[11-13] The paradigm of early infarct-related arterial reperfusion leading to preserved left ventricular function and enhanced survival soon became established and the search for more rapid and sustained methods of coronary artery recanalization began. To determine whether treating the underlying stenosis would improve clinical outcome, a randomized study of intracoronary streptokinase versus primary angioplasty was performed in patients presenting with acute myocardial infarction.[27] Although this study demonstrated improved left ventricular function in patients treated with primary angioplasty,[27] the resources required to maintain 24-hour on-call catheterization facilities limited its widespread clinical use, particularly after the improvements in survival with intravenous thrombolytic agents were established.[1,2] Therefore, potential benefits notwithstanding, primary angioplasty entered a state of relative hibernation in the late 1980s, with some suggesting that the procedure had been prematurely "buried alive."[28]

Nonrandomized Series

Although the use of intravenous thrombolysis increased markedly after its approval for clinical use by the Food and Drug Administration in the late 1980s, some clinical centers aggressively continued to perform primary angioplasty in patients with acute myocardial infarction; these single-center series demonstrated that high procedural success rates (86% to 99%) are attainable with primary angioplasty.[14-21] In a summary of 2,073 patients undergoing primary coronary angioplasty at 10 clinical centers, an aggregate mortality rate of 8.3% was reported.[29] Emergency coronary bypass surgery was performed in 4.9% of patients and recurrent ischemia developed in 4.0%.[29] Comparison of the cumulative results of these angioplasty studies with the results obtained after intravenous thrombolytic administration is problematic, because patients in the nonrandomized series were often selected for angioplasty on the basis of known contraindications to thrombolysis (cardiogenic shock, age ≥75 years, symptom duration ≥6 hours, previous coronary bypass operation, risk of stroke or bleeding, or nondiagnostic electrocardiogram).[8,14,30] A greater risk of procedural mortality with angioplasty has been shown in patients having 1 or more contraindications to thrombolysis.[14] In addition, other underlying demographic and cardiac factors,[8] which can increase case complexity, are often noted in those undergoing primary angioplasty.[31] In 1 series,[14] the in-hospital mortality rate was 3.9% in patients who were candidates for thrombolytic therapy and 24.0% in those who had 1 or more contraindications to such therapy. Bleeding complications were also higher in those patients who were not candidates for thrombolytic administration (10.9% vs 4.9%; $p < 0.001$).[14]

Several factors associated with in-hospital mortality after primary coronary angioplasty have been identified in these nonrandomized series, including the development of cardiogenic shock, the location

of the left anterior descending artery infarct, and the failure to reestablish coronary perfusion.[29] Factors affecting late mortality include prior myocardial infarction, overall diminished left ventricular function, multivessel coronary artery disease, and infarct-related artery patency at discharge.[29] These conditions appear to contribute more to the overall prognosis after myocardial infarction than does the method used to achieve coronary reperfusion.

Randomized Series

At least 5 randomized trials have compared primary angioplasty with thrombolytic therapy in patients with acute myocardial infarction (Table I).[9,10,22,23,27] One of these studies used *intracoronary* streptokinase;[27] the other studies used currently available *intravenous* thrombolytic agents (t-PA, duteplase, and streptokinase). The inclusion criteria, duration of symptoms, and endpoints used in these trials vary substantially (Table I, II); taken together, however, they suggest that primary angioplasty may have certain advantages over thrombolytic therapy in selected acute myocardial infarction patients (Table II, III).

Recurrent Ischemia. None of the current randomized trials have enrolled sufficient numbers of patients to document a comparative benefit of primary angioplasty over thrombolytic therapy in reducing mortality after myocardial infarction. Therefore, the failure of any of these studies to identify a reduction in mortality rates should not be surprising or of particular concern (Table II). To surmount mortality-based sample size limitations, a composite endpoint of death and recurrent myocardial infarction has been used to demonstrate a reduction in recurrent ischemia after primary angioplasty.[9,10] Smaller stud-

TABLE I. Treatment Strategies, Duration of Symptoms, and Concomitant Medications in Randomized Primary PTCA Trials

Author Treatment	Number of Patients	Duration of Pain for Inclusion (h)	Duration of Chest Pain (min)	Concomitant Medications				
				Aspirin (mg)	Heparin	Nitrates	β Blocker	Calcium Antagonists
O'Neill W, et al[27]	56			325	IV x 7-10 d	IV x 24 h	±	Nifedipine
Primary PTCA	29	<12	180 ± 72					
IC streptokinase (4000 U/min)	27	<12	216 ± 108					
Grines CL, et al[9]	395			325 (C)	IV x 3-5 d	IV x 24 h	±	Diltiazem
Primary PTCA	195	<12	181 ± 119					
IV t-PA (100 mg over 3 hr)	200	<12	197 ± 150					
Zijlstra F, et al[10]	142			300	IV x 48 h	IV	±	±
Primary PTCA	70	<6*	167 ± 165					
IV streptokinase (1.5 mU over 60 min)	72	<6*	162 ± 145					
Gibbons RJ, et al[22]	103			162.5 (C)	IV x 5 d	±	+	Avoided
Primary PTCA	47	<12	<4 h (35 pts)					
IV duteplase (0.6 mg/kg x 4 hr)	56	<12	<4 h (43 pts)					
Ribeiro EE, et al[23]	100			325	IV x 48 h	±	±	Diltiazem
Primary PTCA	50	<6	—					
IV streptokinase (1.2 mU over 60 min)	50	<6	—					

C = chewable; IC = intracoronary; IV = intravenous; PTCA = percutaneous transluminal coronary angioplasty; t-PA = tissue plasminogen activator

+ Indicates that patients received this treatment by protocol unless contraindicated
± Indicates that treatment was left to the discretion of the investigator

*Includes patients presenting within 6 to 24 hours of symptom onset with evidence of ongoing ischemia

TABLE II. Procedural Outcome in Randomized Primary PTCA Trials

Author Treatment (No. of Pts.)	Time to Treatment (min)	Time to Reperfusion (min)	PTCA Success (%)	Procedural Outcome				
				Death n (%)	MI n (%)	LVEF (%)	Bleeding n (%)	Residual % Stenosis
O'Neill W, et al[27] (n = 56)								
Primary PTCA	—	246 ± 84	83	2 (6.9)	1 (3.4)	Δ8 ± 7[a]	9 (31.0)	43 ± 31
IC streptokinase (4000 U/min)	—	288 ± 102		1 (3.7)	1 (3.7)	Δ1 ± 6[a]	6 (22.2)	83 ± 17
Grines CL, et al[9] (n = 395)								
Primary PTCA	60	290 ± 174[b]	97	5 (2.6)[c]	5 (2.6)	53 ± 13	0[d]	NA
IV t-PA (100 mg over 3 hr)	32	354 ± 241[b]		13 (6.5)*	13 (6.5)*	53 ± 13	3 (2.0)[d]**	NA
Zijlstra F, et al[10] (n = 142)								
Primary PTCA	61 ± 22	—	98	0	0	51 ± 11	2 (3)	36 ± 20[e]
IV streptokinase (1.5 mU over 60 min)	30 ± 15	—		4 (6)	9 (13)†††	45 ± 12†††	6 (8)	76 ± 19†††
Gibbons RJ, et al[22] (n = 103)								
Primary PTCA	277 ± 144	—	93	2 (4.3)	7 (15)	53 ± 12	—	—
IV duteplase (0.6 mg/kg x 4 hr)	232 ± 174	—		2 (3.6)	20 (36)	50 ± 11	—	—
Ribeiro EE, et al[23] (n = 100)								
Primary PTCA	238 ± 112	—	80	3 (6)	4 (8)[f]	59 ± 13	0	74[g]
IV streptokinase (1.2 mU over 60 min)	179 ± 98†††	—		1 (2)	5 (10)	57 ± 13	0	80

IC = intracoronary; IV = intravenous; MI = myocardial infarction; LVEF = left ventricular ejection fraction; PTCA = percutaneous transluminal coronary angioplasty; t-PA = tissue plasminogen activator

[a] Change in left ventricular ejection fraction from infarction to 7-day catheterization
[b] Time to resolution of chest pain
[c] The combined endpoint of death plus MI was significantly reduced in patients treated with primary angioplasty (5.1% vs 12.0%; p = 0.02).
[d] Intracranial hemorrhage only
[e] Angiography performed 21 ± 31 days after treatment in the streptokinase group and 82 ± 67 days after PTCA in the angioplasty group
[f] Recurrent ischemia
[g] Patency rates within 48 hours

* p <0.10; ** p = 0.05; † p <0.05; †† p <0.01; ††† p <0.005

ies have failed to show a reduction in recurrent ischemia as a secondary endpoint, probably due to limited sample sizes.[22,23]

In the Primary Angioplasty in Myocardial Infarction (PAMI) trial,[9] 395 patients with symptoms of myocardial infarction for less than 12 hours in duration were randomly assigned to treatment with primary angioplasty or intravenous t-PA, 100 mg over 3 hours (Table II). The primary composite clinical endpoint of in-hospital death and recurrent myocardial infarction was significantly lower in the primary angioplasty group (5.1% vs 12.0% in the t-PA group; p = 0.02). In a subgroup of patients stratified as "not low risk" (because of anterior wall myocardial infarction, age ≥75 years, or heart rate >100 beats/min), death or recurrent myocardial infarction was also significantly lower with primary angioplasty (2.0% vs 10.4% with t-PA; p = 0.01). In the Dutch Primary Angioplasty Trial,[10] 142 patients were randomly assigned to treatment with primary angioplasty (n = 70) or intravenous streptokinase, 1.5 mU over 60 minutes (n = 72). Recurrent myocardial infarction occurred less often after primary angioplasty (0% vs 13% in streptokinase-treated patients; p <0.003), and recurrent unstable angina was also less frequent in patients treated with primary angioplasty (6% vs 19% in streptokinase-treated patients; p = 0.02).

TABLE III. Conclusions of Randomized Trials of Primary PTCA and Thrombolytic Therapy in Acute Myocardial Infarction

Author	Stated Conclusions
O'Neill W, et al[27]	• Intracoronary streptokinase and primary PTCA produce similar rates of early coronary perfusion. • Primary PTCA more effectively alleviates the underlying stenosis, resulting in more effective preservation of left ventricular function than that achieved by thrombolytic therapy.
Grines CL, et al[9]	• Primary PTCA reduces the combined occurrence of nonfatal reinfarction or death and is associated with lower rates of intracranial hemorrhage. • Primary PTCA produces no benefit in overall left ventricular systolic function.
Zijlstra F, et al[10]	• Immediate PTCA is associated with a higher rate of patency in the infarct-related artery, a less severe residual stenosis, better left ventricular function, and less recurrent myocardial ischemia and infarction than streptokinase.
Gibbons RJ, et al[22]	• Primary angioplasty does not appear to result in greater myocardial salvage than does the administration of a thrombolytic agent.
Ribeiro EE, et al[23]	• Intravenous streptokinase may be preferred over direct PTCA in patients with acute myocardial infarction.

PCTA = percutaneous transluminal coronary angioplasty

Other beneficial effects of primary angioplasty found in these studies include reductions in the following: need for in-hospital coronary angioplasty,[10] occurrence of any in-hospital complications,[10] recurrence of ischemic events,[9] and need for readmission after hospital discharge.[9] The findings strongly suggest that primary angioplasty reduces recurrent ischemia after myocardial infarction; this benefit is particularly profound in patients who are at high risk for postinfarction morbidity and mortality.

Myocardial Preservation. In some studies,[10,27] but not all,[9,22,23] more improvement of left ventricular function has been shown in patients who have undergone primary angioplasty than in those who have received thrombolytic therapy. In 1 report,[10] global left ventricular ejection fraction at the time of hospital discharge was significantly higher in patients treated with primary angioplasty (51% ± 11% vs 45% ± 12% in streptokinase-treated patients; p = 0.004); other studies have failed to demonstrate a similar improvement (Table II, III). These somewhat disparate findings suggest either that the incremental benefit of primary angioplasty on the preservation of left ventricular function is small or that the global left ventricular ejection fraction is an insensitive index for left ventricular salvage, possibly due to hyperkinesia of noninfarct-zone regional wall motion during the postinfarction period.

As an alternative to assessing global left ventricular function, technetium-99m isonitrile has been used in clinical studies to document the degree of myocardial salvage and to assess overall infarct size after myocardial infarction.[32,33] Infarct size, as determined by technetium-99m isonitrile or sestamibi imaging, has been correlated with left ventricular ejection fraction and regional wall motion both at the time of discharge from the hospital and late following myocardial infarction.[34-36] In a randomized study of 108 patients presenting less than 12 hours after symptom-onset of acute myocardial infarction,[22] 56 were treated with duteplase (0.6 mU/kg body weight over 4 hours) and 52 underwent primary angioplasty. In the 103 patients with primary endpoint analysis, no significant differences in myocardial salvage of the left ventricle (assessed using sestamibi imaging) were noted in the 2 treatment groups (15% ± 19% for t-PA–treated patients and 13% ± 19% for patients undergoing primary angioplasty; p = 0.64). Myocardial salvage of the left ventricle was also similar in the 2 groups of patients with anterior wall infarction (27% ± 21% vs 31% ± 21%, respectively; p = 0.61). Although the sample size is relatively small, this study suggests that the beneficial effect of primary angioplasty on myocardial salvage may be smaller than can be detected using currently available methods of radionuclide imaging.[22]

Bleeding Complications. One advantage of primary angioplasty is the avoidance of systemic fibrinolysis occurring as a result of thrombolytic administration; thus, the low but often disabling risk (<1%) of intracranial hemorrhage may be reduced. Indeed, the incidence of intracranial hemorrhage was lower with primary angioplasty in comparison with thrombolytic therapy (t-PA) in 1 study (0% vs 2%, respectively; p = 0.05).[9] Of note, the need for transfusions and the overall risk of bleeding were similar in the 2 groups, most likely due to complications at the access site after primary angioplasty.[9,10,23]

Residual Stenosis. Compared with thrombolytic therapy, primary coronary angioplasty reduces residual stenosis in the infarct-related artery,[10,27] although little difference between the 2 has been noted in overall vessel patency 48 hours after treatment.[23] The residual % diameter stenosis late after treatment was 76% ± 19% in streptokinase-treated

patients (determined at follow-up angiography after 21 ± 31 days) and 36% ± 20% in angioplasty-treated patients (follow-up angiography at 82 ± 67 days).[10] By reducing residual stenosis, the reinfarction and recurrent symptoms that generally require readmission may occur less often.[9,10]

Unresolved Issues

In aggregate, these randomized trials provide important justification for the use of primary angioplasty as an alternative to thrombolytic therapy in selected patients with acute myocardial infarction (Table III). Nevertheless, several crucial issues remain that may affect the use of primary angioplasty as the definitive strategic approach in such patients.

Obtaining "Normal" Coronary Perfusion. In the angiographic substudy of the Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries (GUSTO) trial,[37] 90-minute patency in the infarct-related artery (TIMI grade 2 or 3) was obtained in 81% of patients treated with "front-loaded" t-PA (100 mg over 90 min) followed by intravenous heparin.[37] These patency rates are higher than those observed after standard t-PA (≈ 70%) and intravenous streptokinase (≈ 60%), which were used in the randomized trials of primary coronary angioplasty. Whether the higher patency rates obtained with front-loaded t-PA would negate some of the beneficial effects of primary angioplasty is not known. Conversely, increasing evidence suggests that restoration of TIMI grade 3 flow is the appropriate therapeutic goal of reperfusion, given the worse prognosis of patients with TIMI grade 2 flow.[38,39] More often than thrombolytic therapy (including front-loaded t-PA), primary angioplasty results in full restoration of TIMI-3 flow, because it also treats the underlying stenosis. Therefore, it is critical that future trials compare primary angioplasty and thrombolytic therapy on the basis of their ability to achieve "normal" coronary perfusion after acute myocardial infarction.

Minimizing Time Delays. Although significant delays were documented in the time to initial treatment of patients randomized to primary angioplasty versus intravenous thrombolytic administration,[9,10,22] the time to reperfusion (i.e., resolution of chest pain) in 1 study[9] was 64 minutes shorter in patients undergoing primary angioplasty. The beneficial effect of primary angioplasty was almost certainly due to the rapid (approximately 60 min) transfer of patients from the emergency room to the catheterization laboratory. The time delay in these studies was much shorter than the 84-minute period preceding immediate angioplasty in the TIMI trial.[5] Precise synchronization of a number of elements is required to achieve this rapid transport from the emergency department to the catheterization laboratory. These factors include in-hospital cardiovascular technical support, cardiologist and cardiovascular surgeon availability within 30 to 45 minutes of notification by the emergency room personnel, established protocols to administer concomitant drug therapy and to facilitate transport, and a sufficient volume of patients to ensure that all personnel remain familiar with the protocol. Given these requirements, a strong commitment on the part of the physicians and hospital staff is required to perform primary coronary angioplasty effectively and expeditiously.

Regional Availability. It is estimated that of the 6,634 hospitals in the continental United States, 1,537 (23.2%) have cardiac catheterization facilities and 825 (12.4%) have coronary bypass surgical facilities. Although some centers have reported that coronary angioplasty may be performed safely without on-site surgical facilities,[40,41] the physiologic complexity of patients presenting with acute myocardial infarction may render primary coronary angioplasty without surgical backup hazardous; approximately 5% of patients are referred to immediate coronary bypass surgery because of high-risk anatomy and another 3% are referred due to complications of coronary angioplasty. Thus, a minority of hospitals in the United States currently have the ability to perform primary coronary angioplasty, and a strategic approach to the triage of patients to tertiary facilities should be evaluated in certain geographic areas.

Economic Considerations. By lowering reocclusion rates,[9,10] promoting early ambulation, reducing the need for ancillary functional studies, and shortening the overall length of hospital stay for acute myocardial infarction patients,[9,22] the use of primary angioplasty rather than thrombolytic therapy may reduce hospital costs.[22] Moreover, follow-up charges may also be lower as a result of fewer readmissions for recurrent ischemia,[22] most likely attributable to the lower residual % diameter stenosis achieved with primary angioplasty.[10,27]

In the Mayo Clinic series reported by Gibbons and colleagues,[22] the length of hospital stay (analyzed by intention-to-treat) was significantly shorter in patients undergoing primary angioplasty (7.7 ± 2.9 days vs 10.6 ± 8.1 days in patients treated with duteplase; $p = 0.01$). This reduced length of stay resulted in a trend toward lower overall in-hospital costs for primary angioplasty patients ($16,811 ± $8,827 vs $21,400 ± $14,806 for duteplase-treated patients; $p = 0.09$) and total 6-month costs ($17,292 ± $8,967 vs $24,129 ± $18,806, respectively; $p = 0.09$). In the PAMI trial,[9] the average length of stay was also significantly shorter in patients treated with primary angioplasty (7.5 ± 8.4 days vs 8.4 ± 4.6 days in t-PA treated patients; $p = 0.03$), presumably due to a lower incidence of recurrent ischemia in patients treated with primary angioplasty (10.3% vs 28.0%, respectively; $p < 0.001$).[9]

Optimal Candidates for Primary Angioplasty

High-Risk Patients. Patients at the highest risk for morbidity and mortality with acute myocardial infarction receive the most benefit from primary coronary angioplasty, provided that reperfusion can be established within 60 to 120 minutes after presentation. Included in this group of patients are those with anterior wall myocardial infarction, those who are elderly (age >70 years), and those with evidence of extensive myocardial necrosis manifested by persistent sinus tachycardia (heart rate >100 beats/min).

Contraindications to Thrombolytic Agents. Patients in whom thrombolysis is contraindicated may also be treated effectively with primary coronary angioplasty.[8,30] Absolute and relative contraindications to thrombolysis include uncontrolled hypertension (diastolic pressure >110 mmHg), gastrointestinal or recent cerebrovascular bleeding, prolonged cardiorespiratory resuscitation, and anticoagulant therapy or known bleeding diathesis.[30] Procedural success with angioplasty can still be expected in more than 90% of these patients.

Cardiogenic Shock. In patients with cardiogenic shock complicating acute myocardial infarction, administration of thrombolytic agents has had little or no mitigating effect on in-hospital mortality.[1,42] In the Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI) trial,[1] patients presenting with Killip IV congestive heart failure[43] showed no benefit from streptokinase administration; the overall mortality rate was 70.1% in placebo-treated patients versus 69.9% in streptokinase-treated patients.[1] Since these sobering results were reported, primary angioplasty has been used instead of or combined with thrombolytic therapy in several nonrandomized series.[44-46] An in-hospital mortality rate of 44% after coronary angioplasty in patients with acute myocardial infarction complicated by cardiogenic shock has been reported.[47] After hospital discharge, a 2.3-year survival rate of 80% has been observed in 1 series.[47]

Assessment of the Benefits of Primary Angioplasty

Delays in Access to Catheterization Facilities. The maximum allowable length of time from diagnosis to primary angioplasty to achieve significant improvement in myocardial preservation compared with thrombolytic therapy has not been determined, although the available evidence suggests that delays of more than 120 minutes may negate most of the comparative benefit of primary angioplasty over thrombolytic therapy. Therefore, when on-site facilities are not available for the patient with an extensive myocardial infarction (≥3-lead ST segment elevation), primary angioplasty may be preferable to thrombolytic therapy—provided that the patient can be transported to a tertiary facility within 120 minutes. Such rapid transfers often require the use of helicopter transport services.

Patients with Prior Coronary Bypass Surgery. Thrombolytic administration may be less effective than primary coronary angioplasty in patients who have had prior coronary bypass surgery than in those who have not, although experience with thrombolytic therapy in this subset of patients is limited.[48,49] Of all patients presenting with acute myocardial infarction, 12% have undergone prior coronary artery bypass grafting.[50] In a series of 72 such patients, primary angioplasty was performed successfully in saphenous vein grafts in 41 of 48 patients (80%) and in the native coronary arteries in all of the remaining 24 patients (100%).[50] The in-hospital survival rate was 90%, including a 64% survival in the patients presenting with cardiogenic shock (15%). Improvement of left ventricular function was also noted during the in-hospital period (from 44% ± 16% to 51% ± 18%; $p < 0.01$). Although the technical approach used in patients with acute myocardial infarction due to an acutely occluded saphenous vein graft varies little from that used in patients with native coronary artery occlusion, diffusely diseased saphenous vein grafts may have an increased thrombus burden and a greater tendency toward distal embolization and "no reflow" after primary angioplasty.[50] Therefore, aggressive mechanical dilatation, prolonged and aggressive anticoagulation with heparin, and adjunct intragraft thrombolytic therapy have been advocated.[50] As an alternative to recanalization of a diffusely diseased saphenous vein graft, coronary angioplasty of the diseased or occluded native coronary artery may be considered.[50]

"Stuttering" Chest Pain Late (6 to 24 hr) after Symptom-Onset. One important step in evaluating patients with acute myocardial infarction is identification of the precise time of symptom-onset. During cyclic reperfusion and reocclusion, some patients report having a "stuttering" chest pain over the preceding 6 to 24 hours. Patients who present late (6 to 24 hr) after symptom-onset have a worse prognosis than do those presenting earlier in the course of myocardial infarction.[1,2] Indeed, the survival benefits attained with thrombolytic therapy in this subgroup of patients are also less pronounced than in those presenting less than 6 hours after symptom-onset,[1,2] although late beneficial effects in left ventricular remodeling may occur in some patients.[51] As an alternative treatment, primary angioplasty has several potential but unproven advantages in patients presenting late after symptom-onset with a stuttering chest pain syndrome. In those patients with totally or subtotally occluded coronary arteries, primary angioplasty may be used to resolve the residual cor-

onary stenosis mechanically. In a series of 24 consecutive patients presenting within 24 hours of the onset of chest pain and undergoing primary coronary angioplasty, 67% demonstrated some residual flow to the infarct-related territory at the time of initial catheterization. Primary angioplasty was successful in 96% of these patients; the mean left ventricular ejection fraction improved from 50% ± 15% to 54% ± 14% during the in-hospital period ($p < 0.05$), and was independent of the time to reperfusion. Another series has demonstrated that the mean left ventricular ejection fraction improved by 14.2% when the reperfusion time was more than 6 hours after the onset of chest pain.[14]

In a study of 139 patients undergoing primary coronary angioplasty late (6 to 48 hr) after symptom onset, the procedure was successful in 78%.[52] The in-hospital mortality rate was 5.5% in association with successful angioplasty and 43% with unsuccessful angioplasty ($p < 0.001$). Multivariate analysis demonstrated that the independent predictors of mortality included cardiogenic shock ($p < 0.001$), unsuccessful angioplasty ($p = 0.001$), an ejection fraction less than 30% ($p = 0.002$), and patient age ($p = 0.004$); the time to angioplasty was not an independent predictor of mortality. Unsuccessful coronary angioplasty was also associated with a particularly high mortality rate in patients with an anterior wall infarction or with an ejection fraction less than 30%.[52] Notably, 2 of the 6 patients who died had evidence of hemorrhagic myocardial infarction consistent with late reperfusion injury.[52]

Poor Candidates for Primary Angioplasty

Primary coronary angioplasty may be less useful than thrombolytic therapy in patients with smaller myocardial infarctions (≤2-lead ST segment elevation) due to the limited amount of myocardial salvage needed, or when a delay of more than 120 minutes to reach a catheterization laboratory is anticipated. In addition, patients who present late (12 to 24 hr) after symptom-onset but do not have evidence of ongoing myocardial ischemia are unlikely to benefit from either primary angioplasty or thrombolytic therapy. Finally, some acute myocardial infarction patients (5%) are identified by angiography immediately; however, primary angioplasty should not be performed in those with significant (>50%) unprotected left main coronary artery disease, diffuse triple-vessel coronary artery disease, or high-risk coronary anatomy. The likelihood of procedural failure is greater in such patients and the prognosis is therefore less favorable.

The use of primary coronary angioplasty as the preferred treatment strategy in patients with acute myocardial infarction depends on a number of factors related to the institutional requirements for maintaining 24-hour on-call catheterization facilities and physician backup. Although the benefits of reduced recurrent ischemia and the potential for improvement of left ventricular function with primary angioplasty are compelling, they must be measured against the increased direct and indirect institutional costs of maintaining such high-technology support. There is little question that the choice between primary angioplasty and thrombolytic therapy must be tailored to the specific requirements of both the patient and the institution initiating treatment. Of paramount importance is the timely treatment of the patient with acute myocardial infarction, allowing maximal benefit from either early pharmacologic reperfusion or mechanical recanalization of the infarct-related artery.

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